# Online resource 4

**Global epigenetic profiling identifies methylation subgroups associated with recurrence-free survival in meningioma**

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## Survival analyses with copy number aberrations (CNA)

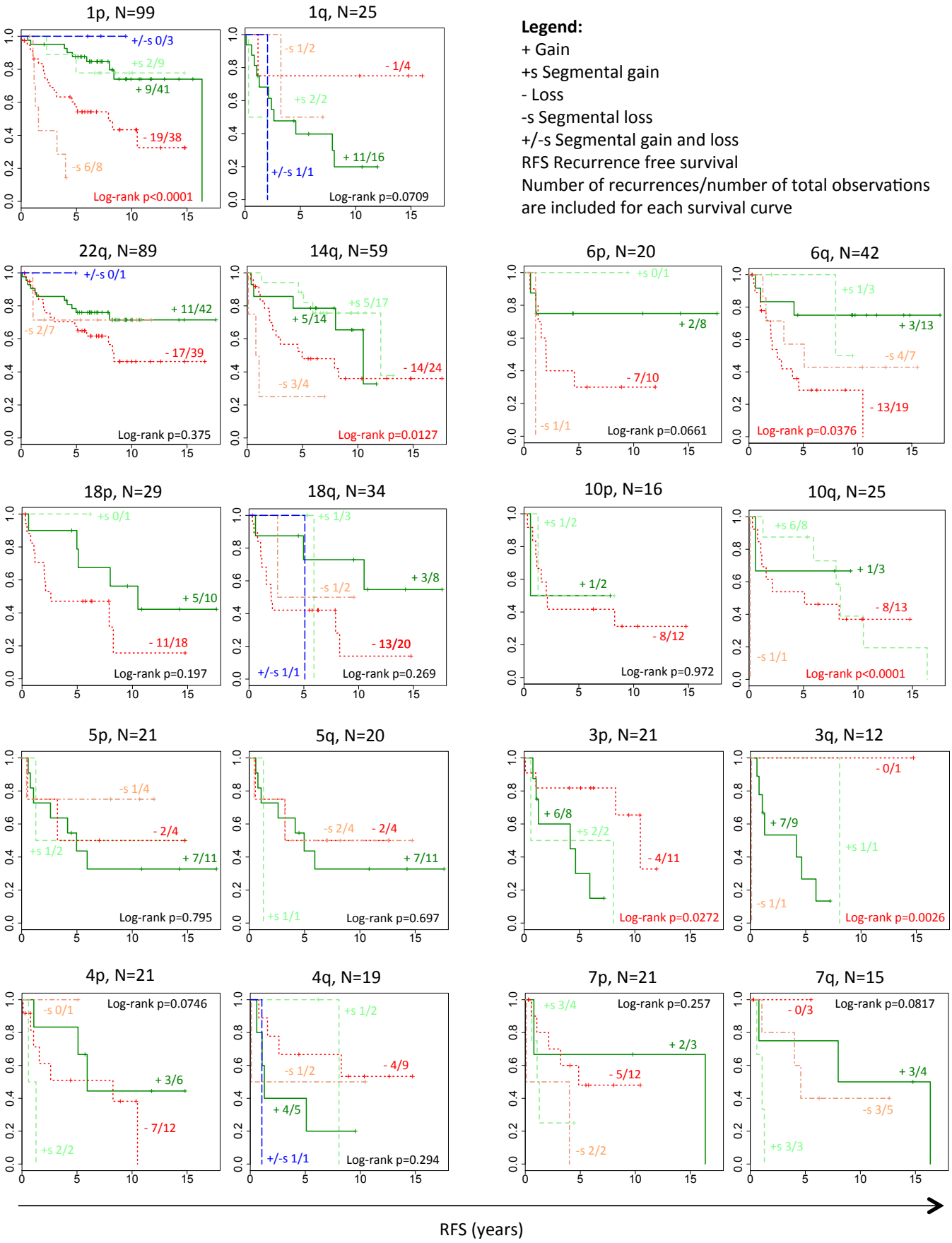
| Chromosomal arm | Number of CNAs overall |
|---|---|
| 1p | 99 |
| 22q | 89 |
| 14q | 59 |
| 6q | 42 |
| 18q | 34 |
| 18p | 29 |
| 1q | 25 |
| 10q | 25 |
| 3p | 21 |
| 4p | 21 |
| 5p | 21 |
| 7p | 21 |
| 5q | 20 |
| 6p | 20 |
| 4q | 19 |
| 13q | 17 |
| 10p | 16 |
| 20q | 16 |
| 2p | 15 |
| 7q | 15 |
| 8q | 15 |
| 12p | 15 |
| 20p | 15 |
| 8p | 14 |
| 9p | 14 |
| 12q | 13 |
| 19p | 13 |
| 3q | 12 |
| 11p | 11 |
| 17q | 11 |
| 2q | 10 |
| 9q | 10 |
| 15q | 10 |
| 16p | 9 |
| 16q | 9 |
| 21q | 9 |
| 19q | 8 |
| 11q | 7 |
| 17p | 5 |

In order to understand the impact the segmental chromosomal gains and losses have on patient outcome (see Figures 1 and 2 in manuscript) and if there are major differences between gains/losses and segmental gains/losses survival analyses for individual chromosomal arms were performed.

For analyses we selected the chromosomal arms with the highest number of copy number aberrations (CNA) (≥20) in the entire dataset (n=137) and their associated chromosomal arm pair (pained in blue in the table to the left).

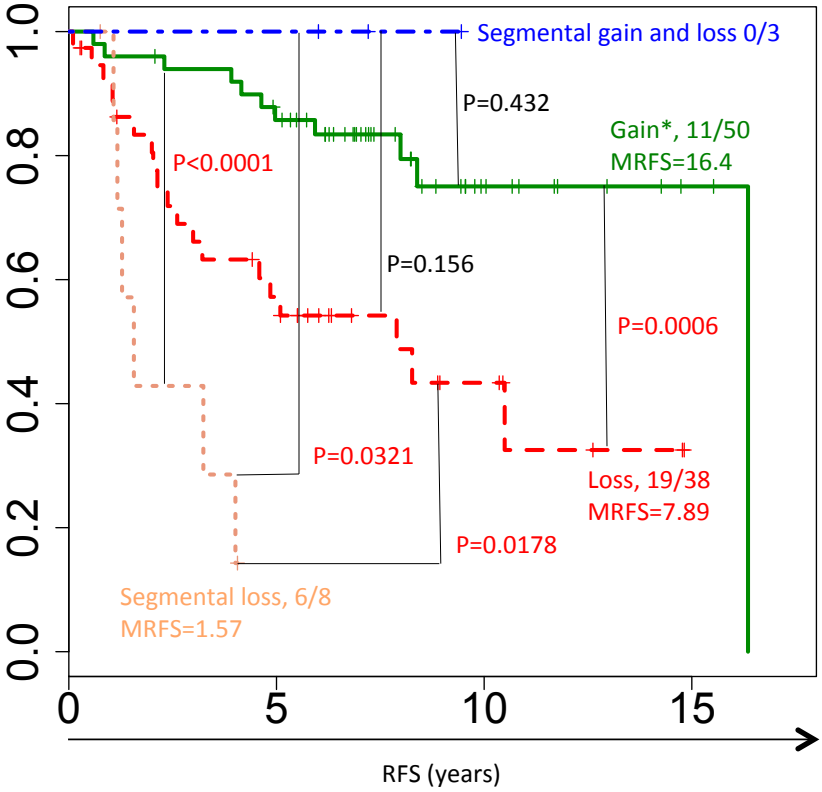
Based on these individual chromosomal arm analyses (see next page for Kaplan-Meier plots in Fig. O.R.4.1) and the relative low number of samples with segmental gains/losses we concluded that in our dataset there are no major survival differences between whole chromosomal arm gain/loss and segmental chromosomal arm/gain and these were grouped for subsequent analyses (i.e. gain and segmental gain were grouped as a single category called *gain;* loss and segmental loss were grouped as a single category called *loss*). The number of samples with combined segmental gain and loss were to few (n=7) to draw conclusions.

# Fig. O.R.4.1 - Detailed survival analyses for patients with selected CNAs



## Detailed survival analysis for meningioma patients with 1p CNAs (n=99)

**Fig. O.R.4.2** - Patients with tumors with segmental 1p loss had significantly decreased recurrence-free survival compared to patients with tumors with 1p loss. (* segmental 1p gains and 1p gains are grouped together). Number of recurrences/number of total observations are included for each survival curve. MRFS – median recurrence free survival; P-value is the log-rank test.

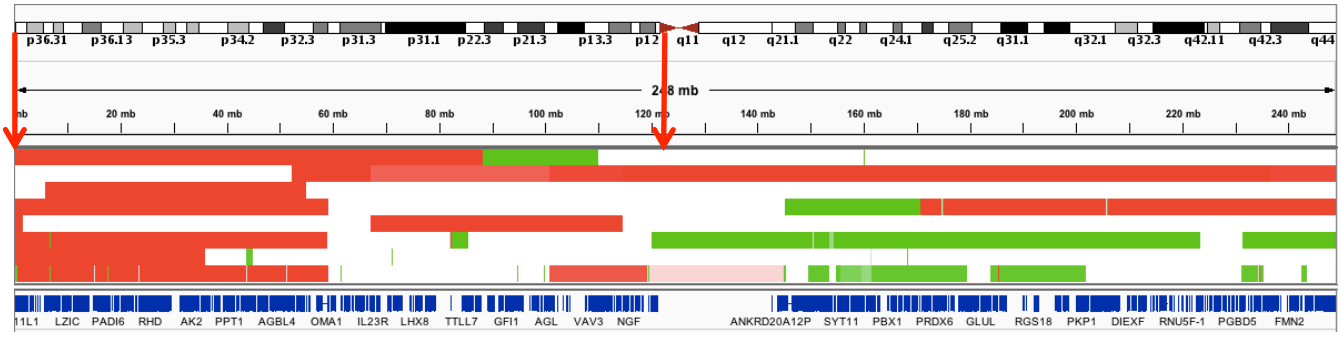


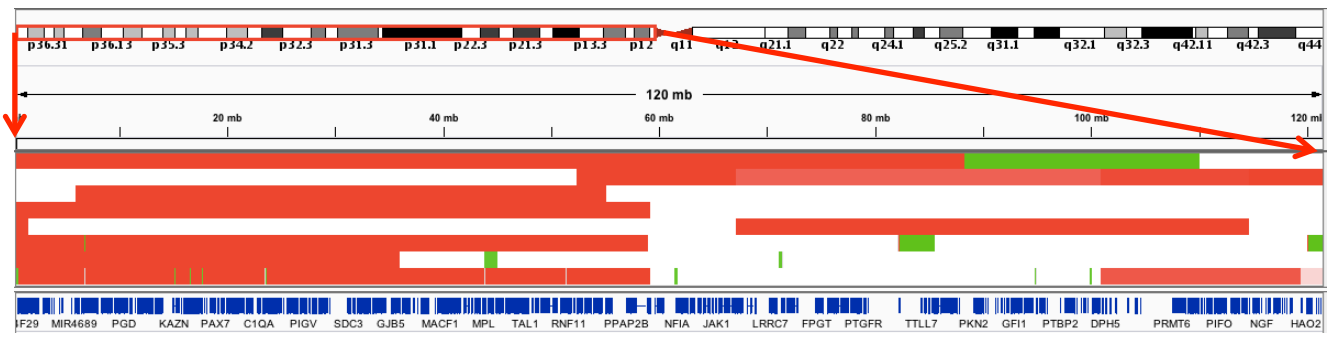

The segmental 1p losses involved the following regions:

- -1p36.33p32.2
- -1p31.3p13.2
- -1p36.33p32.1
- -1p36.33p22.3
- -1p36.31p32.3
- -1p32.3q44
- -1p36.33p34.3
- -1p36.33p32.2

**Fig. O.R.4.3 - Samples (n=8) with segmental 1p loss visualized in Integrative Genomics Viewer (IGV)**

The 1p arm is indicated between red arrows. Each row/line represents a sample. Red - loss, green - gain



## CNA grouping for uni- and multivariable analyses

**Fig. O.R.4.4** – Further, based on findings in Fig. O.R. 3.1. and literature we grouped the following CNAs together: -1p, +1q, -6q, -14q, -18q. In our dataset meningiomas having one or more of these abnormalities were more aggressive, as described in the literature [1] and we further called these CNAs, **aggressive CNAs (aCNAs).**

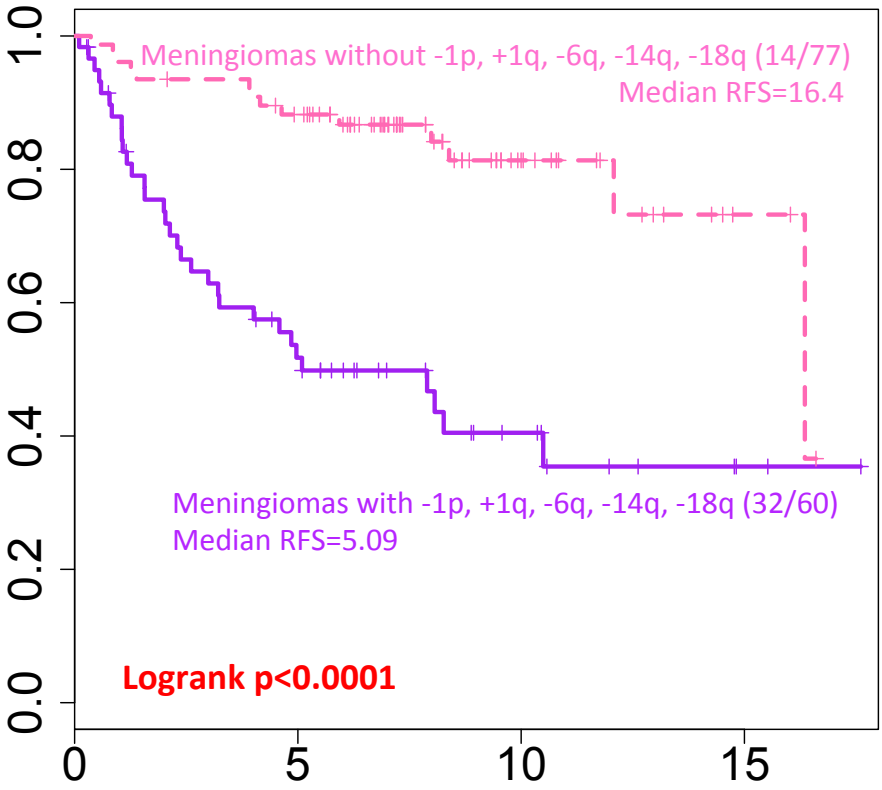
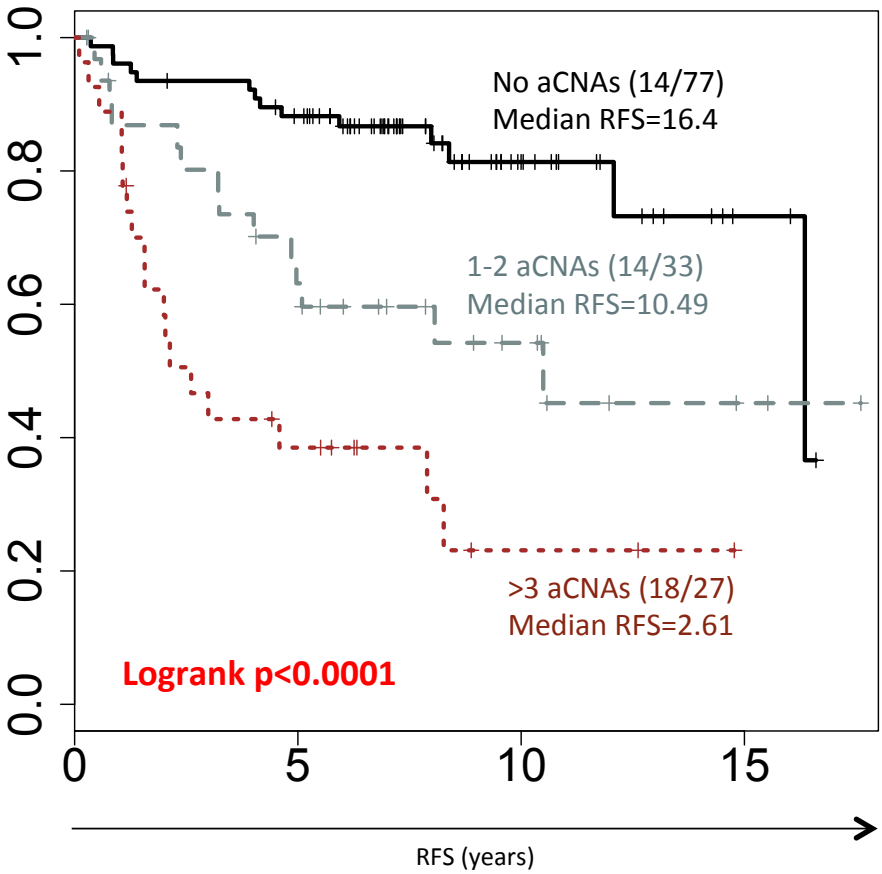



**Fig. O.R.4.5** – When stratified by the number of aCNAs (range: 0 to 5), patients with meningiomas having more than 3 aCNAs had significantly decreased RFS times. This variable was further introduced in uni- and multivariable analyses.




**Refrerence:**

1. Louis DN, Ohgaki H, Wiestler OD, Cavenee WK, Ellison DW, Figarella-Branger D, et al. WHO Classification of Tumours of the Central Nervous System. 4th revised ed. Lyon (France): IARC; 2016